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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,014	12/12/2003	Audrey Goddard	10466/486	2599

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,014	GODDARD ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/8/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 08/08/05 has been acknowledged.

Claims 22-26 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

Claim Rejections - 35 USC § 101 & 35 USC § 112

Claims 22-26 stand rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the same reasons of record as set forth in the office action mailed on 05/03/05.

Novel biological molecules lack well-established utility and must undergo extensive experimentation. The instant claims are directed to an antibody that binds to the polypeptide shown in Figure 32 (SEQ ID NO:83). The claims also recite that the antibody is monoclonal or humanized. The claims recite that the antibody is an antibody fragment or that the antibody is labeled. However, the instant specification does not teach any significance or functional characteristics of the PRO0361 polypeptide (SEQ ID NO:83) or antibody. The specification does not even disclose if PRO0361 is a secreted protein or a transmembrane protein. The specification also does not disclose any specific methods or working examples for the production of the antibody or labeling of the antibody. Since the utility is not presented in mature form and significant further research is required, the utility is not substantial.

The specification asserts the following as patentable utilities for the claimed putative antibody against PRO0361 polypeptide (SEQ ID NO:83): 1) to detect PRO0361 polypeptide expression in specific cells, tissues, or serum 2) as a therapeutic for treatment of various disorders; and 3) for purification of PRO0361 from recombinant cell culture or natural sources

1) to detect PRO0361 *polypeptide expression in specific cells, tissues, or serum.* This asserted utility is not specific or substantial. Such assays can be performed with any antibody. Further, the specification discloses nothing specific or substantial for the PRO0361 polypeptide that is detected by this method. Such an assay is merely to determine the significance of the protein to which the claimed antibody binds, which clearly is of the type of experimentation that does not meet the requirements of 35 USC § 101.

2) as a therapeutic for treatment of various disorders. This asserted utility is not specific or substantial. The specification discloses nothing about the normal level of

expression of the PRO0361 polypeptide. Additionally, the specification does not disclose any disorders, which are associated with altered levels or forms of the PRO0361 polypeptide. Significant further research would be required of the skilled artisan to identify individuals with such a disease. Since the asserted utility is not presented in a ready to use, real-world application, the asserted utility is not substantial.

3) for purification of PRO0361 *from recombinant cell culture or natural sources.* This asserted utility is not specific or substantial. Such methods can be performed with any antibody. Further, the specification discloses nothing specific or substantial for the PRO0361 polypeptide that is purified by this method. Such a method is merely to determine the significance of the protein to which the claimed antibody binds, which clearly is of the type of experimentation that does not meet the requirements of 35 USC § 101.

Therefore, the asserted utility is not substantial, as the real-world use has not been established. Thus, the proposed use of the claimed antibodies that bind PRO0361 polypeptides are simply starting points for further research and investigation into potential uses of the polypeptides. See Brenner v. Manon, 148 U.S.P.Q. 689 (Sup. Ct, 1966), wherein the court held that: *The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public fro an invention with substantial utility:, "[u]nless and until a process is refined and developed to this point- where specific benefit exists in currently available form- there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[I]t is not a reward for the search, but compensation for its successful conclusion."* The only immediate apparent utility for the instant invention would be further scientific characterization of PRO361 polypeptide and an antibody that binds to this protein.

Claims 22-26 stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention for the same reasons of record as set forth in the office action mailed on 05/03/05.

The instant specification does not comply with 35 U.S.C. 101 and 112 since nebulous expressions "biological activity" and "biological properties" do not contain a sufficiently explicit indication of usefulness of compounds and how to use them. The utility requirements must be met at the time of filing and not after someone else identify a utility that had not been disclosed in the specification. <u>The disclosure is insufficient where experimentation is necessary to determine actual uses, or possible lack of uses, of compounds, as well as how to employ them in a useful manner.</u> For example, it cannot be presumed that a steroid chemical compound is "useful" under 35 U.S.C. 101, or that one skilled in the art will know "how to use" it, simply because compound is closely related only in a structural sense to other steroid compounds known to be useful (In re Kirk and Petrow, 153 USPQ 48 (CCPA 1967)).

In instant case the mere presence of mucin protein-like structure does not teach one skill in the art how to use the invention as claimed, since the disclosure is insufficient and requires further experimentation necessary to determine actual uses or possible lack of uses of the polypeptide, as well as how to employ them in a useful manner. It cannot be presumed that an antibody to PRO361 polypeptide is useful under 35 USC 101/112 or that one skilled in the art will know "how to use" it, simply because polypeptide is closely related only in a structural sense to other mucin-like proteins known to be useful. Therefore, the asserted use for the claimed invention is not supported by either a specific and/or substantial utility, since no function can be ascribed to the gene product. The only immediate apparent utility for the instant invention would be further scientific characterization of PRO361 polypeptide and an antibody that binds to this protein.

Response to Arguments and Declaration of Sherman Fong.

The applicant arguments and *S. Fong's declaration* regarding utility and enablement issues has been fully considred. The applicant argues that example 34, found on page 141 discloses that the PRO361 polypeptide tested positive in the Mixed Lymphocyte Reaction (MLR) Assay. The applicant argues that a positive reaction in the MLR assay illustrates that PRO361 functions as an inhibitor of the proliferation of stimulated T-lymphocytes. Similary the declaration submitted by *S Fong*, states that there are specific immune stimulant utilities for the compounds identified by an MLR assay because some PRO polypeptides do the reverse, and give inhibition of T-cell proliferation in the MLR assay. The declaration states that a PRO polypeptide shown to inhibit T-cell proliferation in the MLR assay where the activity is observed as 80% or less of the control, as specified in the present application, would be expected to find practical utility when an inhibition of the immune response is desired, such as in autoimmune diseases. The declaration furhter states that that the MLR assay of the present application is designed to meassure the ability of a test substance to "drive" the dendritic cells to induce the prolifiration of T-cells that are activated or co-stimulated in the MLR assay to identify immunomodulators. The declartion furhter states that like IL-12 the PRO polypeptide has shown to stimulate T-cell proliferation in the MLR assay, therefore there is a practicle utility for the invetion as claimed. The The concluded that if an applicant has asserted that the claimed invention is useful for any particular practical

purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed.

However, applicant's argumetns are found not persuasive. The ability of a protein to stimulate lymphocyte proliferation in the MLR assay does not support a specific and substantial utility for the claimed invention. The ability to stimulate or inhibit lymphocyte proliferation in the MLR assay is an artificial *in-vitro* system and does not provide for what specific conditions or for which specific diseases the claimed invention would predictably function. The assertion that the claimed invention could be useful for the treatment of conditions where the enhancement of the immune response would be beneficial is not specific, since there are many such conditions, and it is not predictable of which conditions the claimed invention may function, if any. Mixed lymphocyte culture (MLC or MLR) is a special case of antigen stimulation in which T lymphocytes respond to foreign histocompatibility antigen on unrelated lymphocytes or monocytes. MLC is a functional assay of cellular response to stimulatory determinants associated predominantly with HLA class II molecules. A single genetic locus or region, known as HLA, controls the MLC reactivity. The MLC assay recognizes disparate HLA class II molecules and the resulting T-cell activation, which is thought to represent an *in vitro* model of the afferent arm of the *in vivo* allograft reaction. The degree of reactivity observed correlates with the degree of antigenic disparity between responding and stimulating cells. Briefly, when the lymphocytes of 2 HLA-disparate individuals are combined in tissue culture, the cells enlarge, synthesize DNA, and proliferate, whereas HLA-identical cells remain quiescent. Since both cells will normally proliferate, a one-way test is used to monitor the response of a single responder cell by inactivating the stimulator cell by radiation or drugs in order to inhibit DNA synthesis of the stimulator cell. The proliferation is driven primarily by the differences in the class II HLA antigens between the 2 test cells (or individuals). This reaction is not predictive of general responses of the immune system because, *in vivo*, activation of a lymphocyte is controlled not only by antigen binding but also by interactions with other cells. All T cells must cooperate with antigen-presenting cells, whereas B cells and cytotoxic T cells depend on helper T lymphocytes. These interactions either require direct surface-to

surface contact or are mediated by cytokines that act only over extremely short distances. Because of this interdependence, lymphocyte activation occurs commonly and efficiently in the secondary lymphoid organs, where lymphocytes, antigens, and antigen-presenting cells encounter one another at close quarters. Therefore, the MLC assay, which is art recognized for determining histocompatibility, does not appear to be predictive of general immune responses *in vivo*. The specification indicates that CD4-IgG was used as a control, but it is not clear how this would control for background stimulation or provide for a measure of maximal stimulation. Lastly, the specification fails to provide any data or evidence of the results of the assay, therefore, one of ordinary skill in the art cannot evaluate the conclusion. The specification states that "positive increases over control are considered positive", however, this does not indicate that statistical significance must occur for determination of a positive result in the assay. Even though the applicant argues that the PRO polypeptide inhibits the lymphocyte proliferation like an IL-12 molecule via dendritic cell interaction the specification fails to provide. Even though the applicant argues that the MLR assay of the present application is designed to meassure the ability of a test substance to "drive" the dendritic cells to induce the prolifiration of T-cells that are activated or co-stimulated in the MLR assay like an IL-12 molecule the specification fails to provide any evidence that PRO polypeptide as claimed is capable of driving the dendritic cells to induce the proliferatiaon of T-cells in the MLR assay via well establishes and specific interaction. In conclusion, the results of the MLR assay do not support a specific and substantial utility for the claimed invention because the assay is not predictive of immune response in general, and one of ordinary skill in the art would not expect a stimulatory effect in the MLC assay to correlate to a general stimulatory effect on the immune system, absent evidence to the contrary. Thus the only immediate apparent utility for the instant invention would be further scientific characterization of PRO361 polypeptide and an antibody that binds to this protein.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

-sk

SUMESH KAUSHAL
PATENT EXAMINER